X-Ray Crystal Structure of 12-Bromoajugarin-I and Conclusion on the Absolute Configuration of Ajugarins

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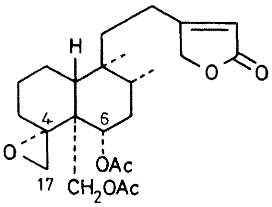
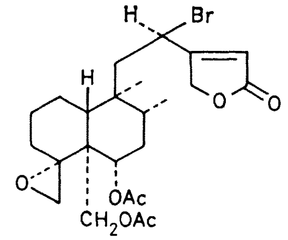
Summary The *X*-ray assignment of 12-bromoajugarin-I provides evidence for the *neo*-clerodane absolute configuration of ajugarins.

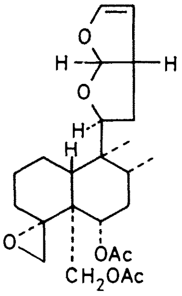
In East Africa the bitter-tasting leaves of *Ajuga remota* (Labiatae) are known not to be attacked by insects. Recently we reported that leaf-disc feeding tests with African army worm, *Spodoptera exempta*, led to the isolation of three antifeedant diterpenes; ajugarin-I, -II, and -III (**1**)—(**3**).[1] These were assigned absolute configurations antipodal to that of clerodin (**4**) based on comparison of c.d. data of the respective 6-oxo derivatives. Recently, the absolute configuration assigned to clerodin was reversed by *X*-ray studies[2] and, accordingly, the ajugarin assignments were revised.[3] However, since the c.d. data for the 6-oxo derivatives of both clerodin and the related diterpene caryoptin led to incorrect configurational assignments for the latter,[2] a reinvestigation of the absolute configuration of the ajugarins appeared advisable. Furthermore, we have now also isolated clerodin from *A. remota* as an antifeedant. The fact that the ajugarins and clerodin, which were assumed to be antipodal, are present in the same plant, provided additional impetus for re-analysing the configuration of the ajugarins and to this end we have carried out an *X*-ray analysis of 12(*R*)-bromoajugarin-I, (**5**), m.p. 148—150 °C, $[\alpha]_D$ −18·1° (*c* 0·12, $CHCl_3$), derived by allylic bromination of the parent material.



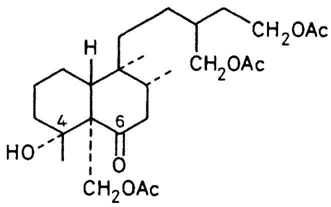
(1) ajugarin-I
(2) ajugarin-II(6-OH)
(3) ajugarin-III(4,17-diol)



(5)



(4)



(6)

Crystal data. monoclinic, $a = 10{\cdot}785(7)$, $b = 9{\cdot}570(5)$, $c = 12{\cdot}354(7)$ Å, $\beta = 103{\cdot}63(5)^\circ$, space group $P2_1$, $Z = 2$. The intensity data for 2317 reflections were collected on a Syntex $R3$ four-circle diffractometer using graphite monochromated Mo-K_α radiation, and an $\omega/2\theta$ scanning technique. A periodically monitored reflection showed no significant crystal deterioration. The structure was determined by the heavy atom method. The hydrogen atoms were located in a difference map computed after block-diagonal least-squares anisotropic refinement of non-hydrogen atoms. The final refinement cycle gave $R = 0{\cdot}092$, in which all hydrogen atoms were included with fixed parameters.† The absolute configuration of the molecule was determined by Bijovet's anomalous-dispersion method based on the observed and calculated structure factors of 20 Friedel pairs. The absolute configuration of the molecule, which is shown in the Figure, matches that of clerodin, ajugarins are, therefore, neoclerodanes like the other members of the clerodin family: they are not antipodal. The negative c.d. sign of the 6-oxo compound (**6**) derived from ajugarin-I[1,4] is, therefore, consistent with the octant rule, the major contributor to the negative Cotton effect being the 5-CH_2OAc. In addition, the 4-methyl and 4-hydroxy groups fall into front octants and compensate each other, while the 8-methyl group and ring-A also compensate each other. On the other hand, the positive c.d. sign of clerodin[4,5] and caryoptin[5] 6-oxo-derivatives must, it seems, be attributed to the hexahydrofurofuran substitution at C-9 on the decalone system. The polarization in the ketone n→π* transitions may be strongly influenced by the non-bonding dipole interaction attributed to the oxygen atoms of hexahydrofurofuran, if the hexahydrofurofuran ring is rotated slightly (see a Dreiding model), the nearest distance between a carbonyl carbon and the furan oxygen becomes 4·5 Å and the axes of the corresponding π* and n orbitals intersect at 2·7 Å from each atom.

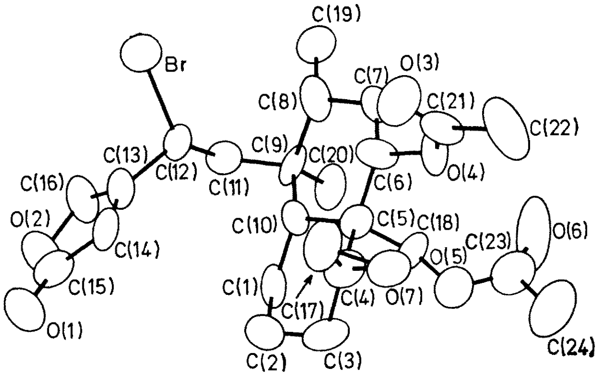


FIGURE. ORTEP drawing of the molecular structure of 12-bromoajugarin-I (**5**).

Thus, we conclude that the negative 6-oxo c.d. of ajugarin-I is correctly based on the octant rule whereas the positive 6-oxo c.d. spectra of clerodin and caryoptin are typical instances of anti-octant behaviour.

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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